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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,291	06/10/2005	Kazufumi Yazaki	Q88235	9414
23373 7590 08/15/2008 SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			EXAMINER MEAH, MOHAMMAD Y	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 08/15/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/538,291

**Applicant(s)**

YAZAKI ET AL.

**Examiner**

MD. YOUNUS MEAH

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 May 2008.  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 4, 10-13 and 16 is/are pending in the application.  
4a) Of the above claim(s) 4 and 10-13 is/are withdrawn from consideration.  
5) ☒ Claim(s) 16 is/are allowed.  
6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

In response to a previous Office action (mailed on 1/10/2008), Applicants filed a response and amendment received on May 09, 2008. Claims 1, 4, 10-13 and 16 are pending. Claim 1 remains withdrawn. Claims 1, 4 and 10 are amended. Claims 4, 10-13 and 16 will be examined.

Applicants' arguments filed on May 09, 2008, and 2008, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### **Claim Rejections**

#### ***35 USC 2nd Paragraph Rejection***

The following is a quotation second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is indefinite in recitation of "wherein the PAL gene is a gene whose expression tends to decrease, by causes other than loss or mutation of the plasmid when introduced into an Escherichia coli other than said selection strain" Since the specification does not define any other PAL gene except genus of plant PAL gene, it is unclear what the recitation means and what characteristics of a PAL gene correlate to

this. How does one identify PAL genes with this property? Whether a gene is stable in a host cell and by what means instability may occur is usually a property of the host cell.

Claim 4 is indefinite in recitation "wherein the initial amount of said PAL gene expression is maintained or enhanced during subculture"- It is unclear how this recitation limits the claimed cell. Claim is to an E. coli strain not to methods of expressing a PAL gene.

#### *IV. 35 U.S.C 103a Rejection*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection of claims 4, 6-7, 10-13 under 35 U.S.C. 103(a) Rowbury et al. (J. appld. Microbiol. 2001, 90, 677-695) in view of Lockwood et al (WO 94/19472, in IDS) and Seaver et al. ( J. Bacteriol. 2001. pp 7182-7189) is withdrawn after finding applicants argument against the use of Rowbury et al. ( J. appld. Microbiol. 2001, 90, 677-695) reference persuasive. However a new 35 U.S.C. 103(a) is applied as shown below.

Claims 4, and 10-13 are rejected under 35 U.S.C. 103(a) Rowe et al. (Appld and Env. Microbiol 1998, 65, 2710-2715) in view of Lockwood et al (WO 94/19472, in IDS) and Seaver et al. (J. Bacterol. 2001, pp 7182-7189)

Claims 4, 6-7, 10-13 are directed to *E. coli* strain expressing any exogenous gene encoding PAL protein, wherein said strain is selected by measuring hydrogen decomposition as a stress response factor.

Lockwood et al (WO 94/19472, in IDS) teach expression of genes encoding Pal protein in *E. coli* strain. However Lockwood et al is silent about a correlation between stress response and high an expression of exogenous gene in *E. coli*.

Rowe et al. (Appld and Env. Microbiol 1999, 65, 2710-2715) teach that metabolic stress in *E. coli* increases upon expression of exogenous gene (Page 2710 paragraph 1-2) and trigger the *E. coli* to produce stress related protein. Therefore; there is correlation between increase in production of exogenous protein via overexpressoin of said protein in *E. coli* with increase in metabolic stress of *E. coli*. One knowledgeable in prior art is motivated to find out host *E. coli* cell which would overexpress exogenous gene in order to obtain optimum production of exogenous protein. In view of the correlation disclosed by Rowe et al., a skilled artisan would understand that one way to select such strain is find out it's metabolic stress level. Viable *E. coli* strains having high metabolic stress would be the strains producing the most exogenous protein.

Seaver et al. teach measurement of hydrogen peroxide decomposition activity in growing *E. coli* strain. Seaver also teach that hydrogen peroxide forms in *E.coli* strain when said strain

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shows stress. It is easier to monitor stress response in *E. coli* by measuring the hydrogen peroxide decomposition.

Therefore a person of ordinary skill in the art is **motivated** to use Seaver's method of measuring hydrogen peroxide decomposition activity to select *E. coli* strain expressing high levels of the PAL gene (as taught by Lockwood et al) wherein increase of exogenous gene expression is correlated with increase in stress response of said *E. coli* strain as taught by Rowe et al.

As such it would have been obvious to one of ordinary skill in the art to transform an *E. coli* strain with an exogenous PAL gene (as taught by Lockwood et al) and use Seaver's method of measuring hydrogen peroxide decomposition activity to select an *E. coli* strain having high stress levels and therefore expressing high levels of the protein as taught by Rowe et al. Therefore claims 4, and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowe et al. in view of Lockwood et al (WO 94/19472, in IDS) and Seaver et al. (J. Bacteriol. 2001. pp 7182-7189).

Applicants' argument against Rowbury et al. became moot as the rejection using Rowbury et al. is withdrawn.

Applicants argue that stress response is a defense mechanism and it acts against exogenous material when introduced into a cell. Thus, it would be counter-intuitive to observe a positive correlation between stress response and exogenous gene expression. Applicants' argument is considered but not found persuasive. As explain above Rowe et al. teach that there is a positive correlation between metabolic stress

and exogenous gene expression. High stress response is indicative of high expression activity (expression of an exogenous gene), and thus it is natural to select a strain having high expression activity based on its stress response.

Applicants further argue that stable expression of repeated sub-culturing is different from high activity expression. This is not persuasive because as explain above viable *E. coli* strain having high metabolic stress (i.e., strain having high expression activity (of an exogenous gene) should have stable expression of said protein over a series of subcultures provided that said subset of *E. coli* strain shows high metabolic stress and stay viable.

Applicants' amendment of the claims necessitates the above rejection.

**THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NASHAAT T NASHED can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-1261.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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